AMACR gene

alpha-methylacyl-CoA racemase

Normal Function

The *AMACR* gene provides instructions for making an enzyme called alpha-methylacyl-CoA racemase (AMACR). This enzyme is found in the energy-producing centers in cells (mitochondria) and in cell structures called peroxisomes. Peroxisomes contain a variety of enzymes that break down many different substances, including fatty acids and certain toxic compounds. They are also important for the production (synthesis) of fats (lipids) used in digestion and in the nervous system.

In peroxisomes, the AMACR enzyme plays a role in the breakdown of a fatty acid called pristanic acid, which comes from meat and dairy foods in the diet. In mitochondria, AMACR is thought to help further break down the molecules derived from pristanic acid.

Health Conditions Related to Genetic Changes

alpha-methylacyl-CoA racemase deficiency

Alpha-methylacyl-CoA racemase (AMACR) deficiency is caused by mutations in the *AMACR* gene. This disorder leads to a variety of neurological problems that begin in adulthood, including gradual loss in intellectual functioning (cognitive decline), seizures, and weakness and loss of sensation in the limbs due to nerve damage (sensorimotor neuropathy). Most individuals with AMACR deficiency have an *AMACR* gene mutation that replaces a protein building block (amino acid) called serine with an amino acid called proline at position 52 in the enzyme sequence, written as Ser52Pro or S52P. This mutation results in a lack (deficiency) of functional enzyme. The enzyme deficiency leads to accumulation of pristanic acid in the blood. However, it is unclear how this accumulation is related to the specific signs and symptoms of AMACR deficiency.

other disorders

AMACR gene mutations that result in a lack of functional AMACR enzyme have also been identified in infants with a life-threatening disorder called congenital bile acid synthesis defect type 4. Babies with this disorder have cholestasis, which is a reduced ability to produce and release a digestive fluid called bile. Cholestasis leads to an enlarged liver (hepatomegaly) and irreversible liver disease (cirrhosis) in the first few months of life.

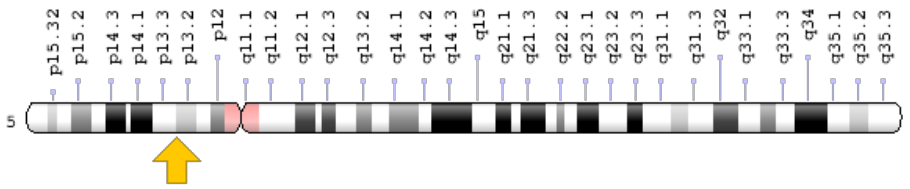
Some researchers consider congenital bile acid synthesis defect type 4 and AMACR deficiency (see above) to be variations of the same disorder. Because most

individuals with congenital bile acid synthesis defect type 4 do not survive infancy, it is unclear whether they would have later developed the neurological symptoms seen in adults with AMACR deficiency.

Chromosomal Location

Cytogenetic Location: 5p13.2, which is the short (p) arm of chromosome 5 at position 13.2

Molecular Location: base pairs 33,986,986 to 34,008,115 on chromosome 5 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- 2-methylacyl-CoA racemase
- AMACR_HUMAN
- AMACRD
- CBAS4
- RACE
- RM

Additional Information & Resources

Educational Resources

- Moecular Biology of the Cell (fourth edition, 2002): Peroxisomes https://www.ncbi.nlm.nih.gov/books/NBK26858/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28AMACR%5BTIAB%5D%29+OR+%28alpha-methylacyl-CoA+racemase%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- ALPHA-METHYLACYL-CoA RACEMASE
  http://omim.org/entry/604489
- BILE ACID SYNTHESIS DEFECT, CONGENITAL, 4
  http://omim.org/entry/214950

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_AMACR.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=AMACR%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=451
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/23600
- UniProt
  http://www.uniprot.org/uniprot/Q9UHK6

Sources for This Summary

- OMIM: ALPHA-METHYLACYL-CoA RACEMASE
  http://omim.org/entry/604489
- Dick D, Horvath R, Chinnery PF. AMACR mutations cause late-onset autosomal recessive cerebellar ataxia. Neurology. 2011 May 17;76(20):1768-70. doi: 10.1212/WNL.0b013e31821a4484.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21576695
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3100132/
- Ferdinandusse S, Denis S, Clayton PT, Graham A, Rees JE, Allen JT, McLean BN, Brown AY, Vreken P, Waterham HR, Wanders RJ. Mutations in the gene encoding peroxisomal alpha-methylacyl-CoA racemase cause adult-onset sensory motor neuropathy. Nat Genet. 2000 Feb; 24(2):188-91.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10655068

- Ferdinandusse S, Denis S, IJlst L, Dacremont G, Waterham HR, Wanders RJ. Subcellular localization and physiological role of alpha-methylacyl-CoA racemase. J Lipid Res. 2000 Nov; 41(11):1890-6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11060359
- Haugarvoll K, Johansson S, Tzoulis C, Haukanes BI, Bredrup C, Neckelmann G, Boman H, Knappskog PM, Bindoff LA. MRI characterisation of adult onset alpha-methylacyl-coA racemase deficiency diagnosed by exome sequencing. Orphanet J Rare Dis. 2013 Jan 3;8:1. doi: 10.1186/1750-1172-8-1.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23286897
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3567975/
- Wierzbicki AS. Peroxisomal disorders affecting phytanic acid alpha-oxidation: a review. Biochem Soc Trans. 2007 Nov;35(Pt 5):881-6. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17956237

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/AMACR

Reviewed: December 2013
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services